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10/509,444

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Gregor Reid

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04/29/2008

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EXAMINER

LEAVITT, MARIA GOMEZ

ART UNIT

PAPER NUMBER

1633

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

| | | | |
|------------------------------|--------------------------------------|------------------------------------|--|
| Office Action Summary | Application No. 10/509,444 | Applicant(s) REID ET AL. | |
| | Examiner MARIA LEAVITT | Art Unit 1633 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 February 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2,4-7,9-15 and 17-20 is/are pending in the application.
- 4a) Of the above claim(s) 6 and 12 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 14,15 and 17-20 is/are rejected.
- 7) ☒ Claim(s) 1,2,4,5,7,9-11 and 13 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

Detailed Action

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 02-04-2008 has been entered.

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
2. Status of claims. Claims 1, 2, 4-7, 9-15 and 17-20 are pending and not claims 1-7, 9-15 and 17-20 as applicants state at page 5 of the Remarks filed on 02-04-2008. Claim 3 has been canceled by Applicant's amendment filed on 02-04-2008, and claims 6 and 12 are withdrawn from consideration by the Examiner as being directed to non-elected species pursuant to 37 CFR 1.14(b), there being no allowable generic or linking claim. This application contains claims 6 and 12 drawn to an invention nonelected with traverse in the reply filed on 12-22-2006. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.
3. The examiner acknowledges that previously filed Exhibits A-D on 07-26-2007 correspond to Figures 3, 4, 8, and Tables 4 and 5 of the Saunders et al., publication, "Disruption of Gardnerella vaginalis biofilms by Lactobacillus," Coll. Surf B: Biointerfaces 2007: 55:138-142; thus Figures 3, 4, 8, as well as Tables 4

and 5 are properly labeled. The Saunders et al., publication filed on 02-04-2008 as Exhibit 3 has been made of record by the examiner on form PTO-892.

4. Therefore, claims 1, 2, 4, 5, 7, 9-11, 13-15 and 17-20 are currently under examination to which the following grounds of rejection are applicable.

Response to Applicant's Remarks

Withdrawn rejections in response to Applicant arguments or amendments

Claim Rejections - 35 USC § 112- Second Paragraph

In view of applicants cancellation of claim 3, rejection of claims 3 under 35 U.S.C. 112, second paragraph, as being indefinite in that it fails to point out what is included or excluded by the claim language, is moot.

In view of applicants arguments and further in light of the guidance provided in the specification and knowledge available to one of ordinary skill in the art at the time of filing, rejection of claim 20 under 35 U.S.C. 112, second paragraph, as being indefinite in that it fails to point out what is included or excluded by the claim language, has been withdrawn.

In view of the withdrawn rejection, applicant's arguments are rendered moot.

5. ***Rejections maintained in response to Applicant arguments or amendments.***

Claim Rejections - 35 USC § 112- First paragraph- Scope of Enablement

Claims 14, 15 and 17-20 remain rejected under 35 U.S.C. 112, first paragraph, because the specification is enabling only for claims limited to:

A method of inhibiting urogenital pathogens colonization of the urogenital tract in women comprising administering a therapeutically effective amount of *Lactobacillus iners* and a pharmaceutically acceptable carrier, wherein said *Lactobacillus iners* is administered orally or vaginally.

The specification does not reasonably provide enablement for a method of maintaining a healthy urogenital flora in females by administering a therapeutically effective amount of at least one *L. iners* by **any route of administration** as recited in claims 14, 19 and 20. Moreover, the specification does not reasonably provide enablement for a method of treatment of **any infection** in a subject as broadly embraced by claim 19.

The instant claims are broadly drawn to a method for maintaining a healthy urogenital flora in females by administering a therapeutically effective amount of *L. iners* by **any route of administration** including parenteral (e.g., intramuscular, intracardiac, subcutaneous, intraperitoneal, intravenous), topical (e.g. skin), and enteral (e.g., mouth) routes. Further, claim 19 broadly embraces **treatment of any disease** by administration of *L. iners* including disease transmitted by bacteria, viruses, fungi and protozoa, upper respiratory tract infections, urinary tract infections, obstetric and perinatal infections, sexually transmitted diseases, lymphomas and leukemias cancer caused by HTLV1 and HTLV2. Specific issues of distribution and generation of immunity in the mucosal urogenital flora have to be considered for the different modes of administration of a pharmaceutically acceptable carrier comprising *L. inners*. Additionally, issues of treating any infectious disease by administration of *L. iners* have to be examined and considered for patentability regarding the broadly claimed methods. The specification as filed discloses that 19 non-symptomatic women were studied to investigate the effect and persistence of vaginally inserted capsules administered for three days containing 1×10^9 CFU viable

lactobacilli: *L. fermentum* RC-14 and *L. rhamnosus* GR-1 (p. 19). Results demonstrated that *L. iners* was detected in the vaginal test samples of the non-symptomatic women. However, no other data is disclosed about administration of viable *lactobacilli* by **any other route**. Moreover, the specification is silent about **treatment of any infection** other than maintaining a healthy vaginal flora by administration of *L. fermentum* RC-14 and *L. rhamnosus* GR-1. Indeed, the specification as filed does not disclose any evidence for a correlation between administration of *L. iners* and reducing or preventing bacterial vaginosis. The art at the time of filing teaches that parenteral routes of administration are not effective on developing a mucosal immune response, whereas oral and topical therapies result in successful treatment of bacterial vaginosis. For example, the art discloses successful maintenance of a normal vaginal flora after oral ingestion of capsules comprising 10^8 viable probiotic lactobacilli (Reid et al., FEMS Immunology and Medical Microbiology, 2001, 37-41; p. 40, columns 1 and 2). In relation to treatment of infectious diseases, the instant claims encompass widely divergent diseases in terms of their pathologic mechanisms. Thus it is unlikely that a treatment effective for diphtheria with antibiotics would also be effective at treating sexually transmitted diseases such as cervical cancer, or AIDS. Additionally, the art discloses that a healthy vagina results from a balance of multiple probiotic *lactobacilli* strains including probiotic strains *L. rhamnosus* GR-1 and *Lactobacillus fermentum* RC-14 (Reid et al., 2001, FEMS, pp 37-41), and *L. iners* AB-1 and *L. crispatus* 33820 (Saunders et al., 2007, Colloids and Surfaces, pp. 138-42). Since a healthy vaginal flora is generated by a balance of *Lactobacillus spp* there is no evidence of record that the sole administration of a *L. iners* reduce or prevent bacterial vaginosis. Hence, it would require undue experimentation to determine alternative regimen of administration meeting the claim

requirements to reduce the risk of bacterial vaginosis in females by administration of a therapeutic effective amount of *L. iners*. Moreover, the specification as filed fails to provide particular guidance to resolve the known unpredictability in the art associated with treatment of **any infection, by any route of administration** of an effective dose of at least *L. iners*. The quantity of experimentation required to practice the methods as claimed would require the *de novo* determination of effective target sites, modes of delivery, safe administration of *L. inners* to target appropriate cells and/or tissues in an infected subject, and further whereby treatment effects are provided for the claimed infection. Since the specification fails to provide particular guidance for any route of administration to treat an infected subject other than for inhibiting urogenital pathogens colonization of the urogenital tract by oral or vaginal administration of a therapeutically effective amount of at least one *L. inners* and the art at the effective time of filing does not disclose treatment of any infection with *L. iners*, it would require undue experimentation to practice the invention as presently claimed. Hence, the scope of the patent protection sought by the Applicant as defined by the claim fails to correlate with the scope of enabling disclosure set forth in the specification.

Response to Applicants' arguments as they relate to rejection of claims 14, 15 and 17-20 under 35 U.S.C. 112, first paragraph.

At page 7 of Remarks, Applicants' argue that it is well known in the art that orally administered *lactobacilli* provide benefits to the respiratory and urinary track; therefore, there is evidence to support that the present invention can provide similar benefits. Moreover, Applicants cite post-filing art of Anukan et al., 2007 as exhibit 1, disclosing that probiotic *lactobacilli* could

boost both the CD4 count in HIV/AIDS patients. As such applicants infer that *L. iners* is effective for treatment of any disease. Such is not persuasive.

Though post filing art of Anukan et al., 2007 teaches that supplementation of conventional yogurt with *lactobacilli* species *L. rhamnosus* GR-1 and *L. reuteri* RC-14 contribute to increase CD4 count in 11/12 HIV/AIDS treated patients in relation to 3/12 in the control, these results are not predictive of all species of *lactobacilli* as each species is genetically distinct resulting in different physiological functionalities. For example, *L. reuteri* produce bacteriocins called reuterin (Talarico and Dobrogosz, Antimicrob Agents Chemother pp. 674-9, 1989), whereas *L. rhamnosus* do not. Similarly, *L. reuteri* RC-14 produce low amounts of hydrogen peroxide, whereas *L. crispatus* 33820 produce high amounts and *L. rhamnosus* GR-1 do not produce at all (Saunders et al., 2007, Colloids Surf B Biointerfaces, Abstract). Likewise, just because one *E. coli* strain causes urinary tract infection, does not mean that the same strain causes diarrhea. On the contrary, there is no such overlap - strains are uropathogenic, or enterotoxigenic, or some are even avirulent and beneficial to the host (Mims et al., Medical Microbiology, 2004, pp. 280-284). Thus, in contrast to applicants' argument there is not factual evidence supporting that orally administered *L. iners* would provide a beneficial treatment of respiratory and urinary track infections, let alone any infection in a subject as broadly encompassed by claim 19.

At page 8 of Remarks, Applicants allege that "administration of *L. iners* can act to reduce the pathogens that ascend from the intestine to the vagina, or in the vagina itself. The *L. iners* can create an environment more conducive to health. Thus, *L. iners* acts on both intestinal and vaginal sites. Several studies, such as Morelli et al. (2004) (copy of the Abstract is enclosed as

Exhibit 4) and Antonio et al. (2005) (copy of the Abstract is enclosed as Exhibit 5), have clearly shown the link between *lactobacilli* in the vagina and intestine”. Additionally, Applicants contend that “the common appearance of *L. iners* in the intestine and vagina makes *L. iners* a perfect choice to one skilled in the art to apply it in both the intestine and vagina. Applicants respectfully submit that the inherent anti-infective and immune modulatory properties of *L. iners* had been well known to one skilled in the art at the time the present application was filed”. As such applicants argue that “one skilled in the art in view of the teaching of the present application together with the well-known knowledge, would not only consider *L. iners* for more widespread therapy but can also use *L. iners* for treating or preventing any infection, without undue experimentation”. Such is not persuasive.

At the outset, the examiner notes that the effective filing date of the present application is March, 28, 2002. The following post filing publications have been submitted by Applicants:

- Exhibit 1. Anukan et al., 2006, Clinical Gastroenterol).
- Exhibit 2. Forum Mother and Baby, 2007.
- Exhibit 3. Saunders et al. 2007 (Colloids Surf. B: Biointerfaces
- Exhibit 4. Morelli et al. (2004) (Abstract)
- Exhibit 5. Antonio et al. (2005) (Abstract)
- Exhibit 6. Kim et al. 2006; (Cellular Microbiology, 2006)
- Exhibit 7. Baroja et al. 2007 (Clinical and Experimental Immunology)
- Exhibit 8. Anukam et al. 2006, (Microbes infect. 2006)

The MPEP § 2164.05(b) recites :

The state of the art existing at the filing date of the application is used to determine whether a particular disclosure is enabling as of the filing date. > Chiron Corp. v. Genentech Inc., 363 F.3d 1247, 1254, 70 USPQ2d 1321, 1325-26 (Fed. Cir. 2004) (“a patent document cannot enable technology that arises after the date of application”). Publications dated after the filing date providing information publicly first disclosed after the filing date generally cannot be used to show what was known at the time of filing. In re Gunn, 537 F.2d 1123, 1128, 190 USPQ 402,405-06 (CCPA 1976); In re Budnick,

537 F.2d 535, 538, 190 USPQ 422, 424 (CCPA 1976) (In general, if an applicant seeks to use a patent to prove the state of the art for the purpose of the enablement requirement, the patent must have an issue date earlier than the effective filing date of the application.). While a later dated publication cannot supplement an insufficient disclosure in a prior dated application to make it enabling, applicant can offer the testimony of an expert based on the publication as evidence of the level of skill in the art at the time the application was filed. *Gould v. Quigg*, 822 F.2d 1074, 1077, 3 USPQ2d 1302, 1304 (Fed. Cir. 1987). [emphasis added]

Though the examiner agrees that submitted post filing references clearly disclose the specific species *L. rhamnosus* GR-1 and *L. reuteri* RC-14 associated with boosting CD4 count (Exhibit 1), treatment of vulvovaginitis with *L. rhamnosus* GR-1 and *L. reuteri* RC-14 (Exhibit 2), first testing of *L. iners* as probiotic in bacterial vaginosis (Exhibit 3), *L. rhamnosus* mediated suppression of TNF produced in macrophages (exhibit 6), *L. rhamnosus* GR-1 and *L. reuteri* RC-14 administration inducing anti inflammatory effect (Exhibit 7) and *L. rhamnosus* GR-1 and *L. reuteri* RC-14 in treatment of bacterial vaginosis (exhibit 8), Applicants submitted references do not show what one skilled in the art knew at the effective filing date of the present application. Indeed, the delivery of *L. iners* in any form as a probiotic to prevent and/or treat urogenital infection has not previously been disclosed in the state of the art at the time of filing. At best, Falsen et al., teaches the discovery of a new species of the genus *Lactobacillus*: *Lactobacillus iners*, isolated from human clinical specimens of the vagina (International Journal of Systematic Bacteriology, 1999, 217-221). However, this disclosure would have not provided sufficient guidance to consider *L. iners* for oral or vaginal probiotic applications, particularly after the unpredictability of the art at the time of filing further illustrated by the use of recombinant *L. iners* merely as deliver vehicle and not as a probiotic strain to treat gastro intestinal track disorders (see Hans et al., particularly, col. 3, line 24, Hans et al., WO01/02570, Publication date

Jan. 11, 2001. Citations are from the National Stage U.S. Patent No. 7,220,418. The National Stage is deemed an English language translation of the PCT). Post filing art further confirms the unpredictability in relation to prevalence of distinct *lactobacilli* species in bacterial vaginosis as evidence by Ferri et al., 2007 (Clin Microbiol. pp. 1016–1018). The author states:

“*L. iners* is rare in grade Ia specimens; however, it is prevalent in grade Ib, a variant of normal, and in grade III, representing BV. The “protective” role of individual vaginal *Lactobacillus* species is unclear. We speculate that *L. iners* is a transitional species and that an *L. crispatus*-predominant species composition represents a stable normal flora” (p. 1018, col. 1, paragraph 2).

As discussed above, and for the reasons of record, the disclosure provided by the applicant is not fully enabled for the scope embraced by the claims because applicant does not provide sufficient guidance to make and use a method for maintaining a healthy urogenital flora in females throughout the life of a woman by administering *L. iners* by **any route, let alone treating any infection in a subject** as embraced and set forth by the invention in light of the guidance provided in the specification and knowledge available to one of ordinary skill in the art.

At page 10 of Remarks, Applicant argue that, in contrast to the examiner assertion, the term “treatment of an infection “as recited in Claim 19 “is clearly defined by the specification at the bottom of page 18 as effective inhibition and prevention of the infection. Moreover, Applicants contend that “the specification defines “therapeutically effective amount” as “an amount of probiotic organism, e.g., *Lactobaeillus iners*, high enough to significantly positively modify the condition to be treated but low enough to avoid serious side effects (at a reasonable benefit/risk ratio), within the scope of sound medical judgment.” See bottom of page 11”. Such is not persuasive.

A preferred embodiment of the instant invention disclosed at page 18 in the specification teaches “nineteen premenopausal Caucasian women, with no symptoms or signs of vaginal or urinary infection and who were otherwise healthy were recruited” no “receiving anti-microbial or any other type of prescribed therapy”. Clearly, Applicants interpretation of the phrase “treatment of an infection” does not contradict a wider interpretation of the phrase such as cure of a disease, amelioration of symptoms of a disease, protection against viral, bacterial or parasitic pathogens, for example. However, the claimed invention is not enabling for treatment of an infection as defined by any of the above therapeutic effects. This is because with regard to claim breadth, the standard under 35 USC § 112, first paragraph, entails the determination of what the claims recite and what the claims means as a whole. In addition, when analyzing the enabled scope of the claims, the teachings of the specification are to be taken into account because the claims are to be given the broadest reasonable interpretation that is consistent with the specification. As such, the broadest reasonable interpretation of claim 19 encompasses a method for prevention and/or restoration to health after an infection, or to bring about recovery from, or remedy by administering a therapeutically effective amount of at least one *Lactobaeillus iners*.

Claim Rejections - 35 USC § 102

Claim 15 is drawn to a pharmaceutical composition comprising *L. iners* and a pharmaceutically acceptable carrier. The as-filed specification defines a “pharmaceutically-acceptable carrier” as any one or more compatible solid or liquid able of being commingled without substantially decreasing the pharmaceutical efficacy of the composition (p. 11). Thus

the pharmaceutical composition can be broadly interpreted as any media that comprises *L. iners* without affecting the efficacy of the composition.

Claim 15 remain rejected under 35 U.S.C. 102(b) as being anticipated by Falsen et al., Journal of Systematic Bacteriology, 1999, 217-221.

Falsen et al., teaches a new isolated species of Lactobacillus: *L. inners* that grows in an agar culture supplemented with 5% horse blood at 37C in air plus CO₂. Clearly, Falsen et al., discloses a prebiotic nutrient utilized by lactobacilli to stimulate and/or enhance growth of lactobacilli relative to pathogenic bacteria, e.g., serum, and a pharmaceutically acceptable carrier, e.g., water. Thus by teaching all the limitations of claim 15, Falsen et al., anticipates the instant invention.

Response to Applicants' arguments as they relate to rejection of claim 15 under 35 USC § 102.

At page 12 of Remarks Applicants argue that “ there are many bacteria types discovered each month, some through growth on blood agar as described in Falsen et al. However, Applicants respectfully submit that the fact that bacteria are kept live on blood agar does not teach or suggest that blood agar can be a prebiotic or good delivery vehicle for humans. Nowhere does the cited reference teach or suggest that the agar mentioned in the reference as either a prebiotic or a pharmaceutical carrier. Indeed, Applicants respectfully submit that blood agar is not a prebiotic, because its contents can be digested in the body and do not require *lactobacilli*. In fact, many organisms, including pathogens, can digest this agar and serum, making these very bad choices for a carrier. As such, one skilled in the art in view of the present application will

recognize that blood agar and serum are not prebiotics or suitable carrier vehicles for lactobacilli application to health”. Such is not persuasive.

As stated in the previous office action, the as-filed specification defines a “pharmaceutically-acceptable carrier” as any one or more compatible solid or liquid able of being commingled without substantially decreasing the pharmaceutical efficacy of the composition (p. 11). The specification as filed defines a prebiotic as “a prebiotic also includes a nutrient utilized by lactobacilli or bifidobacteria to stimulate and/or enhance growth of lactobacilli or bifidobacteria relative to pathogenic bacteria.” (p. 5, paragraph 1). Indeed the culture medium of Columbia Agar Base comprises carbohydrates e.g., corn starch for *L. iners* growth (See, BBL, Columbia Agar, Difco). Applicants have not submitted evidences that *L. iners* could not grow and proliferate in an agar culture media enriched with 5% horse serum blood as demonstrated by the successfully growth in this culture media of *L. iners* taught by Falsen et al.

Claim Rejections - 35 USC § 112- First paragraph- New Matter

Claim 20 remains rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Response to Applicants’ arguments as they relate to rejection of claim 20 under 35 USC § 112- First paragraph- New Matter

At page 14 of Remarks, Applicants argue that the phrase “displacing vaginal pathogens” concerns at least inhibitor displacement and exclusion. Thus, Applicants contend that “based on

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the teaching of the present application, it would be clear to one skilled in the art that Applicants were in possession of the subject matter "displaced vaginal pathogens," either by inhibiting growth or adhesion of the pathogen or excluding the pathogen. See also Saunders et al. Coll. Surf B: Biointerfaces 2007: 55:138-142 and Exhibits A, B and C submitted in the previous response". Such is not persuasive.

The specification as filed teaches at page 7 "the Lactobacillus iners of the present invention will **inhibit growth and/or adhesion of enteric pathogens** to gastrointestinal surfaces", at page 13, paragraphs 2 and 3. Claim 20 is broadly drawn to indigenous-endogenous vaginal pathogens, e.g., originate from within an organism as well as exogenous microorganism, e.g., HIV-1, Herpes and others. Thus the breadth of claim 20 is broader than the guidance provided in the specification. Additionally, it is unclear whether "displacing vaginal pathogens" refers to inhibiting binding or adhesion of other vaginal endogenous pathogens or competing with pathogens already bound to the vaginal mucosa to unbound them. The examiner notes that the purpose of the written description requirement is "to ensure that the inventor had possession, as of the filing date of the application relied on, of the specific subject matter later claimed by him." In reEdwards, 568 F.2d 1349, 1351-52, 196 USPQ 465, 467 (CCPA 1978). Hence, the post-filing art of Saunders et al. 2007, (Coll. Surf B: Biointerfaces pp. 138-142) does not reasonably convey that the inventor had possession of the subject matter of the amendment at the time of the filing of the application,

New grounds of Rejection

New objections/rejections in response to Applicant arguments or amendments:

Claim Objections-Compliance under 37 CFR 1.121(c)

The amendment to the claims filed on 12-18-2007 does not comply with the requirements of 37 CFR 1.121(c) because changes in the texts of currently amended withdrawn claim 13 filed on 02-04-2008 was not completely marked with respect to the previously presented claim 17, filed on 07-26-2007. Specifically, currently amended claim 17 has not been amended, thus it is not identified with the proper status in the claim listing. Amendments to the claims filed on or after 12-18-2007 must comply with 37 CFR 1.121(c) which states:

(c) *Claims*. Amendments to a claim must be made by rewriting the entire claim with all changes (*e.g.*, additions and deletions) as indicated in this subsection, except when the claim is being canceled. Each amendment document that includes a change to an existing claim, cancellation of an existing claim or addition of a new claim, must include a complete listing of all claims ever presented, including the text of all pending and withdrawn claims, in the application. The claim listing, including the text of the claims, in the amendment document will serve to replace all prior versions of the claims, in the application. In the claim listing, the status of every claim must be indicated after its claim number by using one of the following identifiers in a parenthetical expression: (Original), (Currently amended), (Canceled), (Withdrawn), (Previously presented), (New), and (Not entered).

(1) *Claim listing*. All of the claims presented in a claim listing shall be presented in ascending numerical order. Consecutive claims having the same status of “canceled” or “not entered” may be aggregated into one statement (*e.g.*, Claims 1-5 (canceled)). The claim listing shall commence on a separate sheet of the amendment document and the sheet(s) that contain the text of any part of the claims shall not contain any other part of the amendment.

(2) *When claim text with markings is required.* All claims being currently amended in an amendment paper shall be presented in the claim listing, indicate a status of “currently amended,” and be submitted with markings to indicate the changes that have been made relative to the immediate prior version of the claims. The text of any added subject matter must be shown by underlining the added text. The text of any deleted matter must be shown by strike-through except that double brackets placed before and after the deleted characters may be used to show deletion of five or fewer consecutive characters. The text of any deleted subject matter must be shown by being placed within double brackets if strike-through cannot be easily perceived. Only claims having the status of “currently amended,” or “withdrawn” if also being amended shall include markings. If a withdrawn claim is currently amended, its status in the claim listing may be identified as “withdrawn-currently amended.”

(3) *When claim text in clean version is required.* **The text of all pending claims not being currently amended shall be presented in the claim listing in clean version, i.e., without any markings in the presentation of text. The presentation of a clean version of any claim having the status of “original,” “withdrawn” or “previously presented”** will constitute an assertion that it has not been changed relative to the immediate prior version, except to omit markings that may have been present in the immediate prior version of the claims of the status of “withdrawn” or “previously presented.” Any claim added by amendment must be indicated with the status of “new” and presented in clean version, i.e., without any underlining.

(4) *When claim text shall not be presented; canceling a claim.*

(i) No claim text shall be presented for any claim in the claim listing with the status of “canceled” or “not entered.”

(ii) Cancellation of a claim shall be effected by an instruction to cancel a particular claim number. Identifying the status of a claim in the claim listing as “canceled” will constitute an instruction to cancel the claim.

(5) *Reinstatement of previously canceled claim.* A claim which was previously canceled may be reinstated only by adding the claim as a “new” claim with a new claim number

Claim Objection

Claims 1, 9, 13, 14, 19 and 20 are objected to because of the following informalities. Claims 1, 9, 13, 14, 19 and 20 recite the phrase “of at least a *Lactobacillus iners*” which could be interpreted as administering solely one bacterium. The deletion of the phrase “of at least” will help to clarify the meaning of the claims.

Claims 4 and 10 are objected to because of the following informalities: Claims 4 and 10 recite the phrase “further comprising a second probiotic”. Because claims 4 and 10 depend on claims 1 and 9, respectively, one of skilled in the art understand that the second probiotic is administered to the methods of claims 4 and 10. The insertion of the phrase “comprising administering” will help to clarify the meaning of the claims.

Claims 4 and 10 are objected to because of the following informalities: Claims 4 and 10 recite the phrase “a second probiotic”. Claims 4 and 10 depend on claims 1 and 9, respectively. However, claims 1 and 9 do not explicitly recite administering a first probiotic *Lactobacillus iners*. The insertion of the phrase “a first probiotic” will help to clarify the meaning of the claims.

Conclusion

Claims 14, 15 and 17-20 are rejected.

Claims 1, 2, 4, 5, 7, 9-11 and 13 are objected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria Leavitt whose telephone number is 571-272-1085. The examiner can normally be reached on M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, Ph.D can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1633; Central Fax No. (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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/Maria Leavitt/

Maria Leavitt, PhD

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